What is claimed is:

1. A process for decreasing a level of aggregate of pegylated protein isoforms, said process comprising the steps of:

   (a) providing said pegylated protein isoforms; and

   (b) separating said pegylated protein isoforms by anion exchange chromatography using an anion exchange resin under sufficient conditions to decrease said level of said aggregate.

2. The process of claim 1 further comprising the step (a1) of pegylating an unpegylated or a partially pegylated form of said protein, or pegylating both to provide said pegylated protein isoforms.

3. The process of claim 2 wherein said pegylating step (a1) comprises pegylating with free PEG selected from the group consisting of PEG-N-hydroxysuccinimide-5K, PEG-succinimidyl carbonate-5K, PEG-succinimidyl propionate-5K, PEG2-malemide-40K (2 x 20K), PEG2-N-hydroxysuccimide-40K (2 x 20K), and PEG2-aldehyde-40K (2 x 20K).

4. The process of claim 3 wherein a stoichiometric weight ratio of said free PEG to said unpegylated protein is from about 0.5 to about 100.

5. The process of claim 4 wherein said stoichiometric weight ratio is from about 1.5 to about 2.5.

6. The process of claim 5 wherein said stoichiometric weight ratio is from about 1.9 to about 2.

7. The process of claim 6 wherein said stoichiometric weight ratio is from about 1.95 to about 2.05.

8. The process of claim 2 wherein said pegylating step (a1) is conducted at a pegylating pH from about 3 to about 10.

9. The process of claim 8 wherein said pegylating pH is from about 7.2 to about 7.8.

10. The process of claim 9 wherein said pegylating pH is from about 7.4 to about 7.8.

11. The process of claim 10 wherein said pegylating pH is from about 7.40 to about 7.80.

12. The process of claim 2 wherein said pegylating step (a1) is conducted at a pegylating temperature is from about 0 to about 40 °C.

13. The process of claim 12 wherein said pegylating temperature is from about 10 to about 30 °C.

14. The process of claim 13 wherein said pegylating temperature is from about 18 to about 25 °C.

15. The process of claim 1 further comprising an optional HIC step (a2) of selecting said pegylated protein by hydrophobic interaction chromatography (HIC) using an HIC resin.

16. The process of claim 2 further comprising an optional HIC step (a2) of selecting said pegylated protein by hydrophobic interaction chromatography (HIC) using an HIC resin.

17. The process of claim 16 wherein said HIC step (a2) comprises loading said pegylated protein and any unpegylated protein on said HIC resin at an HIC load of less than or equal to about 10 g protein/L of packed bed-volume of HIC resin.

18. The process of claim 17 wherein said HIC load is less than or equal to about 5 g protein/L of packed bed-volume of HIC resin.

19. The process of claim 18 wherein said HIC load is less than or equal to about 4.1 g protein/L of packed bed-volume of HIC resin.

20. The process of claim 17 wherein in said HIC step (a2) said loading is conducted at an HIC loading conductivity from about 30 to about 60 mS/cm.

21. The process of claim 20 wherein said HIC loading conductivity is from about 40 to about 52 mS/cm.

22. The process of claim 21 wherein said HIC loading conductivity is from about 45 to about 51 mS/cm.

23. The process of claim 17 wherein said HIC step (a2) is conducted at an HIC temperature from about 10 to about 40 °C.

24. The process of claim 23 wherein said HIC temperature is from about 15 to about 30 °C.

25. The process of claim 24 wherein said HIC temperature is from about 18 to about 25 °C.

26. The process of claim 16 further comprising a UF/DF#3 step (a3) of ultrafiltering/diafiltering (UF/DF#3) of an eluent from said HIC step (a2).

27. The process of claim 26 wherein said UF/DF#3 step (a3) is conducted with a UF/DF#3 membrane having a UF/DF#3 membrane molecular weight cut-off (MWCO) from about 3 kDa to about 20 kDa.

28. The process of claim 27 wherein said UF/DF#3 membrane MWCO is from about 8 kDa to about 15 kDa.

29. The process of claim 28 wherein said UF/DF#3 membrane MWCO is from about 10 kDa to about 12 kDa.

30. The process of claim 29 wherein said UF/DF#3 membrane MWCO is about 10 kDa.

31. The process of claim 1 wherein said step (b) further comprises a step (b1) of loading said pegylated protein including any impurity and any aggregate thereof on said anion exchange (AEX) resin to provide loaded pegylated protein.

32. The process of claim 31 wherein said AEX resin is selected from the group consisting of ANX4, DEAE, Q-Sepharose, Q-Sepharose FF, Q Sepharose HP, and Q-Sepharose XL.

33. The process of claim 32 wherein said AEX resin is Q-Sepharose FF.

34. The process of claim 31 wherein said step (b1) is conducted at an AEX loading conductivity of less than or equal to about 10 mS/cm.

35. The process of claim 34 wherein said AEX loading conductivity is less than or equal to about 5 mS/cm.

36. The process of claim 35 wherein said AEX loading conductivity is less than or equal to about 2.4 mS/cm.

37. The process of claim 31 wherein said step (b1) is conducted at an AEX loading pH from about 5 to about 10.

38. The process of claim 37 wherein said AEX loading pH is from about 6.6 to about 9.

39. The process of claim 38 wherein said AEX loading pH is from about 6.9 to about 7.1.

40. The process of claim 31 wherein said step (b1) is conducted at an AEX load of pegylated protein including any impurity or said aggregate thereof of less than or equal to about 10 g protein/L of packed bed-volume of AEX resin.

41. The process of claim 40 wherein said AEX load is less than or equal to about 5.5 g protein/L of packed bed-volume of AEX resin.

42. The process of claim 40 wherein said AEX load is less than or equal to about 4.1 g protein/L of packed bed-volume of AEX resin.

43. The process of claim 1 wherein said pegylated protein comprises one or more of said pegylated protein isoforms PEG-1, PEG-2, PEG-3, PEG-4, PEG-5, PEG-6, PEG-7, PEG-

8, and PEG-9 and any aggregate, trisulfide impurity and des-phe impurity thereof and any unpegylated impurity of said protein and any free PEG molecules.

44. The process of claim 1 wherein said pegylated protein comprises one or more of said pegylated protein isoforms PEG-2, PEG-3, PEG-4, PEG-5, PEG-6, PEG-7, PEG-8, and PEG-9 and any aggregate, trisulfide impurity and des-phe impurity thereof and any unpegylated impurity of said protein and any free PEG molecules.

45. The process of claim 1 wherein said pegylated protein comprises one or more of said pegylated protein isoforms PEG-2, PEG-3, PEG-4, PEG-5, PEG-6, PEG-7, PEG-8, and any aggregate, trisulfide impurity and des-phe impurity thereof and any unpegylated impurity of said protein and any free PEG molecules.

46. The process of claim 1 wherein said pegylated protein comprises one or more of said pegylated protein isoforms PEG-3, PEG-4, PEG-5, PEG-6, PEG-7, PEG-8, and any aggregate, trisulfide impurity and des-phe impurity thereof and any unpegylated impurity of said protein and any free PEG molecules.

47. The process of claim 1 wherein said pegylated protein comprises one or more of said pegylated protein isoforms PEG-4, PEG-5, PEG-6, PEG-7, PEG-8, and any aggregate and trisulfide and des-phe impurities thereof and any unpegylated impurity of said protein and any free PEG molecules.

48. The process of claim 1 wherein said pegylated protein comprises one or more of said pegylated protein isoforms PEG-4, PEG-5, PEG-6, PEG-7 and any aggregate, trisulfide impurity and des-phe impurity thereof and any unpegylated impurity of said protein and any free PEG molecules.

49. The process of claim 1 wherein said pegylated protein comprises one or more of said pegylated protein isoforms PEG-4, PEG-5, PEG-6 and any aggregate, trisulfide impurity and des-phe impurity thereof and any unpegylated impurity of said protein and any free PEG molecules.

50. The process of claim 1 wherein said pegylated protein comprises one or more of said pegylated protein isoforms PEG-4, PEG-5, PEG-6 and any aggregate, trisulfide impurity and des-phe impurity thereof and any unpegylated impurity of said protein.

51. The process of claim 1 wherein said pegylated protein comprises one or more of said pegylated protein isoforms PEG-1, PEG-2, PEG-3, PEG-4, PEG-5, PEG-6, PEG-7, PEG-8, and PEG-9 and any aggregate, trisulfide impurity and des-phe impurity thereof.

52. The process of claim 1 wherein said pegylated protein comprises one or more of said pegylated protein isoforms PEG-1, PEG-2, PEG-3, PEG-4, PEG-5, PEG-6, PEG-7, PEG-8, and PEG-9 and any aggregate and trisulfide impurity thereof.

53. The process of claim 1 wherein said pegylated protein comprises one or more of said pegylated protein isoforms PEG-1, PEG-2, PEG-3, PEG-4, PEG-5, PEG-6, PEG-7, PEG-8, and PEG-9 and any aggregate thereof.

54. The process of claim 1 further comprising a pooling step (c) of pooling discrete amounts of said pegylated protein isoforms to yield a pooled pegylated protein by a technique selected from the group consisting of capillary electrophoresis (CE), sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE), ion exchange (IEX) chromatography, hydrophobic interaction chromatography (HIC), anion exchange (AEX) chromatography, cation exchange (CEX) chromatography, reverse-phase high pressure liquid chromatography (RPHPLC), size exclusion high pressure liquid chromatography (SEHPLC), affinity chromatography (AC) and combinations thereof.

55. The process of claim 42 further comprising a pooling step (c) of pooling discrete amounts of said pegylated protein isoforms of said pegylated protein to yield a pooled pegylated protein by a technique selected from the group consisting of capillary electrophoresis (CE), sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE), ion exchange (IEX) chromatography, hydrophobic interaction chromatography (HIC), anion exchange (AEX) chromatography, cation exchange (CEX) chromatography, reverse-phase high pressure liquid chromatography (HPLC), size exclusion high pressure liquid chromatography (SEHPLC), and affinity chromatography (AC) and combinations thereof.

56. The process of claim 54 wherein said pooling step (c) is conducted by said CE at a CE temperature from about 5 to about 50 °C.

57. The process of claim 55 wherein said pooling step 9c) is conducted by said CE at a CE temperature from about 5 to about 50 °C.

58. The process of claim 56 wherein said CE temperature is from about 5 to about 45 °C.

59. The process of claim 58 wherein said CE temperature is from about 20 to about 40 °C.

60. The process of claim 59 wherein said CE temperature is from about 30 to about 32 °C.

61. The process of claim 56 wherein said pooling step (c) is conducted by said CE at a CE pooling conductivity from about 0 to about 60 mS/cm.

62. The process of claim 61 wherein said CE pooling conductivity is from about 5 to about 10 mS/cm.

63. The process of claim 54 wherein said pooling step (c) is conducted on said pegylated protein isoforms provided in a buffer at a protein concentration of at least about 0.2mg/ml.

64. The process of claim 56 wherein said pooling step (c) is conducted on said pegylated protein isoforms provided in a buffer at a protein concentration of at least about 0.5 mg/ml.

65. The process of claim 54 wherein said pooling step (c) is conducted on said pegylated protein isoforms provided in a buffer at a protein concentration from about 0.1 to about 100 mg/ml.

66. The process of claim 65 wherein said protein concentration is from about 0.5 to about 10 mg/ml.

67. The process of claim 66 wherein said protein concentration is from about 2 to about 3 mg/ml.

68. The process of claim 56 wherein said pooling step (c) is conducted on said pegylated protein isoforms provided in a buffer at a protein concentration from about 0.1 to about 100 mg/ml.

69. The process of claim 67 wherein said protein concentration is from about 0.5 to about 10 mg/ml.

70. The process of claim 68 wherein said protein concentration is from about 2 to about 3mg/ml.

71. The process of claim 63 wherein said pooled pegylated protein comprises one or more of PEG-1, PEG-2, PEG-3, PEG-4, PEG-5, PEG-6, PEG-7, PEG-8, and PEG-9.

72. The process of claim 63 wherein said pooled pegylated protein comprises one or more of PEG-2, PEG-3, PEG-4, PEG-5, PEG-6, PEG-7, PEG-8, and PEG-9.

73. The process of claim 63 wherein said pooled pegylated protein comprises one or more of PEG-3, PEG-4, PEG-5, PEG-6, PEG-7, PEG-8, and PEG-9.

74. The process of claim 63 wherein said pooled pegylated protein comprises one or more of PEG-3, PEG-4, PEG-5, PEG-6, PEG-7, and PEG-8.

75. The process of claim 63 wherein said pooled pegylated protein comprises one or more of PEG-3, PEG-4, PEG-5, PEG-6, and PEG-7.

76. The process of claim 63 wherein said pooled pegylated protein comprises one or more of PEG-3, PEG-4, PEG-5, and PEG-6.

77. The process of claim 63 wherein said pooled pegylated protein comprises one or more of PEG-4, PEG-5, and PEG-6.

78. The process of claim 63 wherein said pooled pegylated protein comprises one or more of PEG-4 and PEG-5.

79. The process of claim 63 wherein said pooled pegylated protein comprises one or more of PEG-5, and PEG-6.

80. The process of claim 63 wherein said pooled pegylated protein comprises PEG-5.

81. The process of claim 71 wherein a pooled pegylated protein fraction of PEG-4, PEG-5 and PEG-6 comprises at least about 70% by weight based on a total weight of said PEG-1, PEG-2, PEG-3, PEG-4, PEG-5, PEG-6, PEG-7, PEG-8 and PEG-9 pegylated protein isoforms and any aggregate thereof.

82. The process of claim 71 wherein said pooled pegylated protein fraction of PEG-4, PEG-5 and PEG-6 comprises at least about 75% by weight based on a total weight of said PEG-1, PEG-2, PEG-3, PEG-4, PEG-5, PEG-6, PEG-7, PEG-8 and PEG-9 pegylated protein isoforms and any aggregate thereof.

83. The process of claim 71 wherein said pooled pegylated protein fraction of PEG-4, PEG-5 and PEG-6 comprises at least about 80% by weight based on a total weight of said PEG-1, PEG-2, PEG-3, PEG-4, PEG-5, PEG-6, PEG-7, PEG-8 and PEG-9 pegylated protein isoforms and any aggregate thereof.

84. The process of claim 71 wherein said pooled pegylated protein fraction of PEG-4, PEG-5 and PEG-6 comprises at least about 90% by weight based on a total weight of said PEG-1, PEG-2, PEG-3, PEG-4, PEG-5, PEG-6, PEG-7, PEG-8 and PEG-9 pegylated protein isoforms and any aggregate thereof.

85. The process of claim 71 wherein said pooled pegylated protein fraction of PEG-4, PEG-5 and PEG-6 comprises at least about 94% by weight based on a total weight of said PEG-1, PEG-2, PEG-3, PEG-4, PEG-5, PEG-6, PEG-7, PEG-8 and PEG-9 pegylated protein isoforms and any aggregate thereof.

86. The process of claim 64 wherein said buffer in which said pegylated protein is provided has a pH from about 5 to about 10.

87. The process of claim 86 wherein said buffer has a pH from about 6.6 to about 9.

88. The process of claim 87 wherein said buffer has a pH from about 6.9 to about 7.1.

89. The process of claim 64 wherein said buffer in which said pegylated protein is provided is selected from the group consisting of Tris, phosphate, HEPES, citric acid, triethylamine, and histidine.

90. The process of claim 1 wherein said level of said aggregate is less than or equal to about 10% by weight based on a total weight of said isoforms and said aggregate.

91. The process of claim 90 wherein said level of said aggregate is less than or equal to about 9% by weight based on said total weight.

92. The process of claim 91 wherein said level of said aggregate is less than or equal to about 8% by weight based on said total weight.

93. The process of claim 92 wherein said level of said aggregate is less than or equal to about 7% by weight based on said total weight.

94. The process of claim 93 wherein said level of said aggregate is less than or equal to about 6% by weight based on said total weight.

95. The process of claim 94 wherein said level of said aggregate is less than or equal to about 5% by weight based on said total weight.

96. The process of claim 95 wherein said level of said aggregate is less than or equal to about 4% by weight based on said total weight.

97. The process of claim 96 wherein said level of said aggregate is less than or equal to about 3% by weight based on said total weight.

98. The process of claim 97 wherein said level of said aggregate is less than or equal to about 2% by weight based on said total weight.

99. The process of claim 98 wherein said level of said aggregate is less than or equal to about 1.5% by weight based on said total weight.

100. The process of claim 99 wherein said level of said aggregate is less than or equal to about 1% by weight based on said total weight.

101. The process of claim 100 wherein said level of said aggregate is less than or equal to about 0.9% by weight based on said total weight.

102. The process of claim 101 wherein said level of said aggregate is less than or equal to about 0.8% by weight based on said total weight.

103. The process of claim 102 wherein said level of said aggregate is less than or equal to about 0.7% by weight based on said total weight.

104. The process of claim 103 wherein said level of said aggregate is less than or equal to about 0.6% by weight based on said total weight.

105. The process of claim 104 wherein said level of said aggregate is less than or equal to about 0.5% by weight based on said total weight.

106. The process of claim 105 wherein said level of said aggregate is less than or equal to about 0.4% by weight based on said total weight.

107. The process of claim 106 wherein said level of said aggregate is less than or equal to about 0.3% by weight based on said total weight.

108. The process of claim 107 wherein said level of said aggregate is less than or equal to about 0.2% by weight based on said total weight.

109. The process of claim 108 wherein said level of said aggregate is less than or equal to about 0.1% by weight based on said total weight.

110. The process of claim 109 wherein said level of said aggregate is less than or equal to about 0.05% by weight based on said total weight.

111. The process of claim 110 wherein said level of said aggregate is less than or equal to about 0.01% by weight based on said total weight.

112. The process of claim 31 wherein said step (b) further comprises a step (b2) of washing said loaded pegylated protein followed by a step (b3) of eluting with an eluting solution said loaded pegylated protein by a pH gradient or an ionic strength gradient and a step (b4) of collecting an eluent in multiple volume fractions .

113. The process of claim 31 wherein said step (b) further comprises a step (b2) of washing said loaded pegylated protein followed by an eluting step (b3) of eluting said loaded pegylated protein with a salt solution in an eluting buffer containing an ionic salt at a salt

concentration gradient sufficient to elute said loaded pegylated protein from said AEX resin.

114. The process of claim 113 wherein said ionic salt is a chloride salt.

115. The process of claim 114 wherein said ionic salt is NaCl.

116. The process of claim 115 wherein said step (b) is conducted in a column having a column volume (CV) and wherein said salt concentration gradient is from about 2 to about 50 mM per CV.

117. The process of claim 116 wherein said salt concentration gradient is from about 5 to about 25 mM per CV.

118. The process of claim 117 wherein said salt concentration gradient is from about 10 to about 20 mM per CV.

119. The process of claim 113 wherein said eluting buffer has a pH from about 5 to about 10.

120. The process of claim 119 wherein said eluting buffer has a pH from about 6.6 to about 9.

121. The process of claim 120 wherein said eluting buffer has a pH from about 6.9 to about 7.1.

122. The process of claim 113 wherein said eluting step (b3) is conducted at an eluting temperature of less than or equal to 50 °C.

123. The process of claim 122 wherein said eluting temperature is less than or equal to about 35 °C.

124. The process of claim 123 wherein said eluting temperature is from about 2 to about 30 °C.

125. The process of claim 123 wherein said eluting temperature is from about 15 to about 30 °C.

126. The process of claim 123 wherein said eluting temperature is from about 18 to about 25 °C.

127. The process of claim 113 wherein said step (b) is conducted in a column wherein said eluting buffer has a linear velocity through said column of less than or equal to about 300 cm/hr.

128. The process of claim 127 wherein said linear velocity is from about 10 to about 150 cm/hr.

129. The process of claim 127 wherein said linear velocity is from about 30 to about 150 cm/hr.

130. The process of claim 127 wherein said linear velocity is from about 50 to about 100 cm/hr.

131. The process of claim 127 wherein said linear velocity is from about 50 to about 70 cm/hr.

132. The process of claim 127 wherein said linear velocity is from about 60 to about 65 cm/hr.

133. The process of claim 127 wherein said linear velocity is about 60 cm/hr.

134. The process of claim 1 wherein said pegylated protein is selected from the group consisting of hormone, growth hormone, human growth hormone, growth hormone antagonist, human growth hormone antagonist, an antibody, and B-2036 PEG.

135. The process of claim 1 wherein said anion exchange (AEX) resin comprises functional groups selected from the group consisting of primary, secondary, tertiary, quaternary amines, and combinations thereof.

136. The process of claim 1 wherein said anion exchange (AEX) resin comprises functional groups selected from the group consisting of diethylaminoethyl, diethylaminopropyl, dimethylethanolamine, trimethyl-ammonium-ethyl, trimethylbenzyl ammonium, dimethylethanol benzyl and polyamine functional groups.

137. The process of claim 1 wherein said anion exchange (AEX) resin comprises a support material selected from the group consisting of hydrophilic polyether, crosslinked divinyl benzene polystyrene, crosslinked agarose, polypropylene, hydrophilic acrylamidovinyl, methacrylic, polymerized hydrogel with a ceramic bead base, composite silica-dextran material, polymer grafted silica, divinyl benzene styrene, divinyl benzene polyacrylic, crosslinked cellulose, co-polymer methacrylate, polystyrene, acrylic, G5000 hydrophilic gel, and cellulose.

138. The process of claim 1 wherein said anion exchange (AEX) resin comprises a macroporous resin.

139. The process of claim 1 wherein said anion exchange (AEX) resin comprises a gel resin.

140. The process of claim 63 wherein said pooled pegylated protein consists essentially of one or more of PEG-1, PEG-2, PEG-3, PEG-4, PEG-5, PEG-6, PEG-7, PEG-8, and PEG-9.

141. The process of claim 63 wherein said pooled pegylated protein consists essentially of one or more of PEG-2, PEG-3, PEG-4, PEG-5, PEG-6, PEG-7, PEG-8, and PEG-9.

142. The process of claim 63 wherein said pooled pegylated protein consists essentially of one or more of PEG-3, PEG-4, PEG-5, PEG-6, PEG-7, PEG-8, and PEG-9.

143. The process of claim 63 wherein said pooled pegylated protein consists essentially of one or more of PEG-3, PEG-4, PEG-5, PEG-6, PEG-7, and PEG-8.

144. The process of claim 63 wherein said pooled pegylated protein consists essentially of one or more of PEG-3, PEG-4, PEG-5, PEG-6, and PEG-7.

145. The process of claim 63 wherein said pooled pegylated protein consists essentially of one or more of PEG-3, PEG-4, PEG-5, and PEG-6.

146. The process of claim 63 wherein said pooled pegylated protein consists essentially of one or more of PEG-4, PEG-5, and PEG-6.

147. The process of claim 63 wherein said pooled pegylated protein consists essentially of one or more of PEG-4 and PEG-5.

148. The process of claim 63 wherein said pooled pegylated protein consists essentially of one or more of PEG-5, and PEG-6.

149. The process of claim 63 wherein said pooled pegylated protein consists essentially of PEG-5.

150. The process of claim 31 wherein said step (b) is conducted in a column having a column volume (CV) and wherein said step (b) further comprises a step (b2) of washing said loaded pegylated protein followed by a step (b3) of eluting with an eluting solution said loaded pegylated protein by a pH gradient or an ionic strength gradient and a step (b4) of collecting an eluent in multiple volume fractions from about 0.1 to about 5 of said column volume (CV).

151. The process of claim 31 wherein said step (b) is conducted in a column having a column volume (CV) and wherein said step (b) further comprises a step (b2) of washing said loaded pegylated protein followed by a step (b3) of eluting with an eluting solution said loaded pegylated protein by a pH gradient or an ionic strength gradient and a step (b4) of collecting an eluent in multiple volume fractions from about 0.1 to about 1 of said column volume (CV).

152. The process of claim 31 wherein said step (b) is conducted in a column having a column volume (CV) and wherein said step (b) further comprises a step (b2) of washing said loaded pegylated protein followed by a step (b3) of eluting with an eluting solution said

loaded pegylated protein by a pH gradient or an ionic strength gradient and a step (b4) of collecting an eluent in multiple volume fractions from about 0.1 to about 0.5 of said column volume (CV).

153. The process of claim 31 wherein said step (b) is conducted in a column having a column volume (CV) and wherein said step (b) further comprises a step (b2) of washing said loaded pegylated protein followed by a step (b3) of eluting with an eluting solution said loaded pegylated protein by a pH gradient or an ionic strength gradient and a step (b4) of collecting an eluent in multiple volume fractions from about 0.1 to about 0.2 of said column volume (CV).

154. The process of claim 113 wherein said ionic salt is selected from the group consisting of NaCl, lithium chloride, Na phosphate, Na sulfate, ammonium chloride, ammonium sulfate, ammonium phosphate, KI, and KCl.

155. The process of claim 118 wherein said salt concentration gradient is from about 10 to about 12.5 mM per CV.

156. A process for pooling pegylated protein isoforms, said process comprising the step of:

(a) separating and collecting said pegylated protein isoforms by a technique selected from the group consisting of capillary electrophoresis (CE), sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE), ion exchange (IEX) chromatography, hydrophobic interaction chromatography (HIC), anion exchange (AEX) chromatography, cation exchange (CEX) chromatography, reverse-phase high pressure liquid chromatography (RPHPLC), size exclusion high pressure liquid chromatography (SEHPLC), affinity chromatography and combinations thereof.

157. The process of claim 140 when said technique is RPHPLC or CE.

158. A process for decreasing a level of aggregate of pegylated growth hormone antagonist isoforms having a total weight of said isoforms and said aggregate, said process comprising the steps of:

(a) providing said pegylated growth hormone antagonist isoforms; and

(b) separating said pegylated growth hormone antagonist isoforms on an anion exchange (AEX) resin by anion exchange chromatography under sufficient

conditions to decrease said level of said aggregate to less than or equal to about 6% by weight based on said total weight.

159. The process of claim 158 wherein the conditions are sufficient to decrease said level of said aggregate to less than or equal to about 5% by weight based on said total weight.

160. The process of claim 158 wherein the conditions are sufficient to decrease said level of said aggregate to less than or equal to about 4% by weight based on said total weight.

161. The process of claim 158 wherein the conditions are sufficient to decrease said level of said aggregate to less than or equal to about 3% by weight based on said total weight.

162. The process of claim 158 wherein the conditions are sufficient to decrease said level of said aggregate to less than or equal to about 2% by weight based on said total weight.

163. The process of claim 158 wherein the conditions are sufficient to decrease said level of said aggregate to less than or equal to about 1% by weight based on said total weight.

164. A process for decreasing a total level of a sum of any trisulfide impurity, any des-phe impurity and any aggregate of pegylated growth hormone antagonist isoforms having a total weight of said isoforms, said impurities and said aggregate, said process comprising the steps of:

(a) providing said pegylated growth hormone antagonist isoforms; and

(b) separating said pegylated growth hormone antagonist isoforms on an anion exchange (AEX) resin by anion exchange chromatography under sufficient conditions to decrease said total level of any said trisulfide impurity, any of said des-phe impurity and any of said aggregate to less than or equal to about 15% by weight based on said total weight.

165. The process of claim 164 wherein the conditions are sufficient to decrease said total level of any said trisulfide impurity, any of said des-phe impurity and any of said aggregate to less than or equal to about 12% by weight based on said total weight.

166. The process of claim 164 wherein the conditions are sufficient to decrease said total level of any said trisulfide impurity, any of said des-phe impurity and any of said aggregate to less than or equal to about 10% by weight based on said total weight.

167. The process of claim 164 wherein the conditions are sufficient to decrease said total level of any said trisulfide impurity, any of said des-phe impurity and any of said aggregate to less than or equal to about 9% by weight based on said total weight.

168. The process of claim 164 wherein the conditions are sufficient to decrease said total level of any said trisulfide impurity, any of said des-phe impurity and any of said aggregate to less than or equal to about 8% by weight based on said total weight.

169. The process of claim 164 wherein the conditions are sufficient to decrease said total level of any said trisulfide impurity, any of said des-phe impurity and any of said aggregate to less than or equal to about 7% by weight based on said total weight.

170. The process of claim 164 wherein the conditions are sufficient to decrease said total level of any said trisulfide impurity, any of said des-phe impurity and any of said aggregate to less than or equal to about 6% by weight based on said total weight.

171. The process of claim 164 wherein the conditions are sufficient to decrease said total level of any said trisulfide impurity, any of said des-phe impurity and any of said aggregate to less than or equal to about 5% by weight based on said total weight.

172. The process of claim 164 wherein the conditions are sufficient to decrease said total level of any said trisulfide impurity, any of said des-phe impurity and any of said aggregate to less than or equal to about 4% by weight based on said total weight.

173. The process of claim 164 wherein the conditions are sufficient to decrease said total level of any said trisulfide impurity, any of said des-phe impurity and any of said aggregate to less than or equal to about 3% by weight based on said total weight.

174. The process of claim 164 wherein the conditions are sufficient to decrease said total level of any said trisulfide impurity, any of said des-phe impurity and any of said aggregate to less than or equal to about 2% by weight based on said total weight.

175. The process of claim 164 wherein the conditions are sufficient to decrease said total level of any said trisulfide impurity, any of said des-phe impurity and any of said aggregate to less than or equal to about 1% by weight based on said total weight.

176. The process of claim 134 wherein said growth hormone antagonist is B-2036 PEG wherein said B-2036 PEG comprises a growth hormone antagonist polypeptide backbone of B-2036 of [SEQ. ID NO. 1].

177. The process of claim 134 wherein said growth hormone is a pegylated form of a polypeptide of [SEQ. ID NO. 2].

178. The process of claim 137 wherein said support material has a diameter from about 10 to about 500 μm.

179. The process of claim 178 wherein said diameter has an average of 90 μm.

180. A process for pooling pegylated protein isoforms, said process comprising the steps of:

(a) separating said pegylated protein isoforms into selected isoforms; and

(b) combining said selected isoforms to yield an enriched pool of said selected isoforms.

181. The process of claim 180 wherein said selected isoforms are PEG-4, PEG-5 and PEG-6 with a pool weight ratio of ((a first weight of PEG-4 + PEG-5 + PEG-6)/(a second weight of any PEG-1 + PEG-2 + PEG-3 + PEG-4 + PEG-5 + PEG-6 + PEG-7 + PEG-8 + PEG-9 present in said enriched pool)) which pool weight ratio is greater than or equal to about 70% by weight.

182. The process of claim 181 wherein said pool weight ratio is greater than or equal to about 75% by weight.

183. The process of claim 181 wherein said pool weight ratio is greater than or equal to about 80% by weight.

184. The process of claim 181 wherein said pool weight ratio is greater than or equal to about 85% by weight.

185. The process of claim 181 wherein said pool weight ratio is greater than or equal to about 90% by weight.

186. The process of claim 181 wherein said pool weight ratio is greater than or equal to about 94% by weight.

187. The process of claim 181 wherein said pool weight ratio is greater than or equal to about 95% by weight.

188. The process of claim 181 wherein said pool weight ratio is greater than or equal to about 96 by weight.

189. The process of claim 181 wherein said pool weight ratio is greater than or equal to about 97% by weight.

190. The process of claim 181 wherein said pool weight ratio is greater than or equal to about 98% by weight.

191. The process of claim 181 wherein said pool weight ratio is greater than or equal to about 99% by weight.

192. The process of claim 181 wherein said pool weight ratio is greater than or equal to about 99.5% by weight.

193. The process of claim 181 wherein said pool weight ratio is greater than or equal to about 99.9% by weight.

194. The process of claim 180 wherein said selected isoforms are one or more of PEG-1, PEG-2, PEG-3, PEG-4, PEG-5, PEG-6, PEG-7, PEG-8, and PEG-9.

195. The process of claim 180 wherein said selected isoforms are one or more of PEG-2, PEG-3, PEG-4, PEG-5, PEG-6, PEG-7, PEG-8, and PEG-9.

196. The process of claim 180 wherein said selected isoforms are one or more of PEG-3, PEG-4, PEG-5, PEG-6, PEG-7, PEG-8, and PEG-9.

197. The process of claim 180 wherein said selected isoforms are one or more of PEG-4, PEG-5, PEG-6, PEG-7, PEG-8, and PEG-9.

198. The process of claim 180 wherein said selected isoforms are one or more of PEG-4, PEG-5, PEG-6, PEG-7, and PEG-8.

199. The process of claim 180 wherein said selected isoforms are one or more of PEG-4, PEG-5, PEG-6 and PEG-7.

200. The process of claim 180 wherein said selected isoforms are one or more of PEG-4, PEG-5, and PEG-6.

201. The process of claim 180 wherein said selected isoforms are one or more of PEG-4 and PEG-5.

202. The process of claim 180 wherein said selected isoforms are one or more of PEG-5, and PEG-6.

203. The process of claim 180 wherein said selected isoforms are one or more of PEG-4 and PEG-6.

204. A process for obtaining a selected pegylated protein isoform from a mixture of at lest two pegylated protein isoforms, sand process comprising the step of:

(a) separating said selected pegylated protein isoform from said mixture.